

**Remarks**

This application contains claims 1-131, the status of which is as follows:

(a) Claims 42, 51 53-54, 62-65, 67-70 and 74 are as originally filed.

(b) Claim 40 was previously presented.

(c) Claims 1-3, 5-8, 10-36, 38-39, 41, 43, 45-48, 50, 52, 55-61, 66, 71-73, 75, and 78-80 have been currently amended.

(d) Claims 4, 9, 37, 44, 49, 76-77, and 81-118 have been canceled without disclaimer or prejudice.

(e) Claims 119-131 are new.

No new matter has been added.

Applicant thanks Examiner Bockelman for the courtesy of a personal interview with Applicant's representative, Sanford T. Colb (Reg. No. 26,856), held in the USPTO on November 28, 2007. At the interview, Mr. Colb and the Examiner discussed possible amendments to independent claims 1 and 41, as previously presented, in light of US Patent 6,341,236 to Osorio et al. The Examiner suggested the incorporation of a sensor for sensing heart rate during non-vagal stimulation times and the initiation of the heart rate variability treatment based upon heart rate parameters sensed relative to a desired baseline value.

***Rejections under 35 U.S.C. 102(b) and/or 103(a)***

Claims 5-6, 10, 12-14, 17, 21-26, 29-30, 36, 50, 52-54, 57, 61-66, 69-70, 86, 90-93, 96, and 103-104 were rejected under 35 U.S.C. 102(b) as anticipated by, or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 6,341,236 to Osorio et al. Claims 1-2, 4, 31, 33-35, 41-42, 44, 51, 71, 74, and 75 were

rejected under 35 U.S.C. 103(a) as being unpatentable over Osorio et al. in view of US Patent 5,578,061 to Stroetman et al. Claims 3, 7-8, 11, 15-16, 18-20, 27-28, 32, 38-40, 43, 47-48, 55-56, 58-60, 67-68, 72, 73, 78-85, 87-89, 94-95, 97-102, and 107-108 were rejected under 35 U.S.C. 103(a) as being unpatentable over Osorio et al. Claims 45-46 were rejected under 35 U.S.C. 103(a) as being unpatentable over Osorio et al. in view of US Patent 4,702,254 to Zabara.

### ***Background***

In a previous office action dated July 6, 2006, independent claims 1 and 41 (which had not yet been amended to recite the amplitude of between about 2 and about 10 milliamps) were rejected under 35 U.S.C. 102(b) over Osorio et al. Dependent claims 3, 5-30, 32, 36, 38-40, 43, 45-50, 52-70, 72, 73, and 78-80 were found to recite allowable subject matter. While disagreeing with the rejections of claims 1 and 41, the Applicant chose not to argue on the merits, but rather to expedite the issuance of a patent by amending these independent claims to include the features of allowable dependent claims 9 and 49, respectively, namely an amplitude of between about 2 and about 10 milliamps. In addition, a number of the allowable dependent claims were recast in independent form, incorporating all of the limitations of the parent claim and any intervening claims.

As mentioned above, in the present office action dated September 7, 2007, all of the pending claims have been rejected. The Applicant thus has decided to remove the features of claims 9 and 49 from claims 1 and 41, respectively, re-present canceled claims 9 and 49 as new claims 119 and 125, and traverse the rejection over Osorio et al. of claims 1 and 41 as previously presented.

***Rejections under 35 U.S.C. 102(b) in the previous office  
action***

In the previous office action dated July 6, 2006, claims 1, 2, 4, 31, 33-35, 37, 41-42, 44, 51, 71, and 74-77 were rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 6,341,236 to Osorio et al. The Examiner argued that Osorio et al. teach a vagal stimulation system that applies stimulation to the vagus nerve, monitors the resulting heart rate variability, and, "[i]f the heart rate variability is too great, the microprocessor applies adjusted stimulation . . . to the vagus nerve" (p. 2 of the office action).

While not necessarily agreeing with the Examiner's grounds for rejection, the Applicant has amended claims 1 and 41 as originally filed to recite reducing heart rate variability "below a baseline heart rate variability of the subject when the current is not applied."

Osorio et al. describe a "system and method for using electrical stimulation of the vagus nerve to treat epilepsy with minimized or no effect on the heart" (abstract). Thus, the object of Osorio et al. is to treat epilepsy, while avoiding undesired effects on the heart. Osorio et al. do not describe affecting the heart in order to treat epilepsy or any other condition. Osorio et al. emphasize this object a number of times:

It is an object of the present invention to minimize or eliminate the effects on the heart caused by the electrical stimulation of the vagus nerve 60 (col. 8, lines 32-34, emphasis added).

Accordingly, it is an object of the invention to provide a technique for controlling or preventing epilepsy via stimulation of the vagus nerve with

minimized effect on the heart rate. It is another object of the invention to provide a technique for adjusting the vagus nerve stimulation to minimize its affect on the heart rate (col. 3, lines 6-11, emphasis added).

As discussed herein, it is preferred that the stimulation be accomplished so as to have minimal effect on the heart (col. 5, lines 21-23, emphasis added).

Osorio et al. recognize that their vagal stimulation sometimes undesirably increases heart rate variability. They thus describe techniques for counteracting this undesirable increase in heart rate variability:

Generally, stimulation of the vagus nerve 60 increases heart rate variability (standard deviation) at higher IHR values. It is therefore desirable to provide a technique for vagus nerve stimulation that minimizes or has no effect on the normal operation of the heart as measured by the standard deviation [heart rate variability] of the IHR as a function of the IHR (col. 8, line 65- col. 9, line 4, emphasis added).

Osorio et al. also recognize that their vagal stimulation sometimes undesirably decreases heart rate variability:

Referring still to control algorithm of FIG. 6, once the heart rate variability is determined, the system monitors, at step 620, whether the heart is operating within its normal parameters as illustrated in FIG. 5 by the solid lines in the graph. If it is determined that heart rate variability is too high or too low relative to the IHR for that time period, the stimulation of the vagus nerve 60 is adjusted to bring the heart into its normal heart rate variability

parameters. If the heart rate and/or heart rate variability are maintained within their normal patterns, then no changes to the stimulation are made (col. 9, lines 39-49, emphasis added).

In sum, Osorio et al. teach monitoring and modulating heart rate variability only to minimize undesired changes in heart rate variability caused by vagal stimulation for treating epilepsy. Thus, Osorio et al. neither teach nor suggest configuring their stimulation to reduce heart rate variability below its baseline rate. Indeed, reducing heart rate variability below its baseline rate, as recited in claims 1 and 41, would run counter to Osorio et al.'s stated object of minimizing the effect of their stimulation on the heart.

The Applicant thus submits that claims 1 and 41, as amended, are patentable over Osorio et al., and over Osorio et al. in view of Stroetman et al. All of the remaining pending claims directly or indirectly depend from claim 1 or claim 41, and thus are also in a condition for allowance, being of narrower scope than the allowable claims from which they depend.

The Applicant notes that some embodiments of the claimed invention do not include sensing heart rate variability. In these embodiments, stimulation is applied, e.g., generally constantly or intermittently, and is configured to reduce heart rate variability below baseline, such as using the parameters described on pp. 104-105 of the specification. The stimulation is not necessarily applied responsively to or adjusted responsively to sensed heart rate variability. The Examiner's attention is drawn to the *in vivo* experimental results described with respect to Fig. 6 (p. 108), in which heart rate variability

was reduced substantially below baseline without using sensed heart rate variability for feedback.

### ***Dependent claims***

Although the Applicant believes that all of the dependent claims are allowable because they are of narrower scope than the allowable independent claims from which they depend, in this section the Applicant nevertheless presents arguments for patentability of a portion of the dependent claims.

#### *Claims 120 and 127*

Claims 120 and 127 recite treatment of a condition by reducing the heart rate variability. The Applicant respectfully submits that these claims are patentable over Osorio et al. because Osorio et al. describe configuring the stimulation to reduce (back to baseline) heart rate variability that is artificially and undesirably elevated as a side effect of vagal stimulation for treatment of epilepsy. In contrast, in these claims, the reduction of heart rate variability is itself the treatment.

#### *Claims 122 and 128*

The Applicant respectfully submits that claims 122 and 128 are patentable over Osorio et al. because Osorio et al. clearly do not describe causing a prolonged reduction in heart rate variability below a baseline level. As mentioned above, Osorio et al. lower heart rate variability only on an as-needed basis, when the heart rate variability is artificially and undesirably elevated by the vagal stimulation.

*Claims 124 and 130*

Claims 124 and 130 recite that the current is configured to reduce the heart rate of the subject below a normal heart rate of the subject, in conjunction with reducing heart rate variability. As discussed above regarding heart rate variability, Osorio et al. teach away from such a reduction. The object of Osorio et al. is to avoid causing a change in the heart rate of the subject:

Accordingly, it is an object of the invention to provide a technique for controlling or preventing epilepsy via stimulation of the vagus nerve with minimized effect on the heart rate. It is another object of the invention to provide a technique for adjusting the vagus nerve stimulation to minimize its affect on the heart rate (col. 3, lines 6-11, emphasis added).

As discussed herein, it is preferred that the stimulation be accomplished so as to have minimal effect on the heart (col. 5, lines 21-23, emphasis added).

If the heart rate and/or heart rate variability are maintained within their normal patterns, then no changes to the stimulation are made (col. 9, lines 46-49, emphasis added).

***Claim amendments***

As mentioned above, claims 1 and 41 have been amended to recite that the current is configured to reduce heart rate variability "below a baseline heart rate variability of the subject when the current is not applied." These amendments find support in numerous passages in the specification as filed, including:

In some embodiments of the present invention, the control unit is configured to drive the electrode device

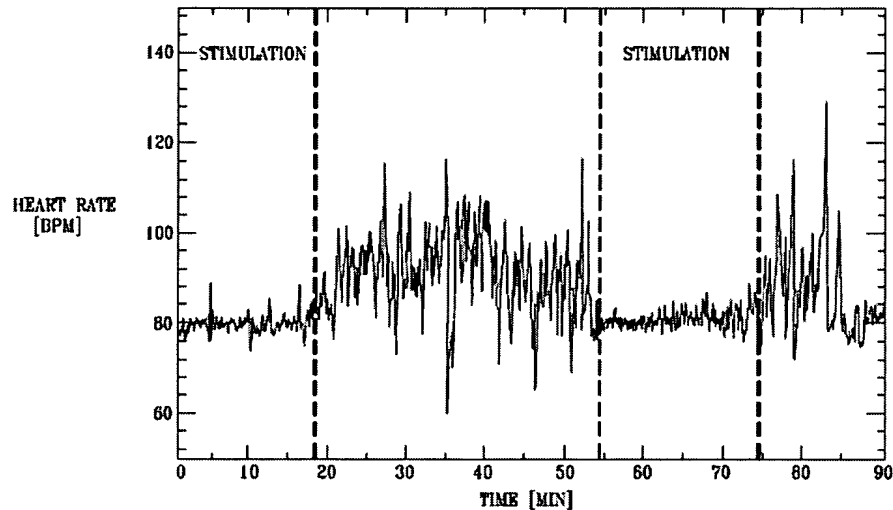
to stimulate the vagus nerve so as to modify heart rate variability of the subject. For some applications, the control unit is configured to apply stimulation with parameters that tend to or that are selected to reduce heart rate variability, while for other applications parameters are used that tend to or that are selected to increase variability. For some applications, the parameters of the stimulation are selected to both reduce the heart rate of the subject and heart rate variability of the subject. For other applications, the parameters are selected to reduce heart rate variability while substantially not reducing the heart rate of the subject. For some applications, the control unit is configured to drive the electrode device to stimulate the vagus nerve so as to modify heart rate variability in order to treat a condition of the subject (p. 27, line 24 - p. 28, line 9).

In an embodiment, the control unit is adapted to configure the current to reduce the heart rate variability by at least 5% below a baseline thereof during a time period in which a heart rate of the subject is not reduced responsive to the current by more than 10% below a baseline thereof (p. 66, lines 26-31).



Fig. 6 shows the result of an in vivo experiment on a dog:

FIG. 6



It can be clearly seen that during the stimulation periods heart rate variability drops substantially below the baseline level. These experimental results are described in the specification:

During a first period and a third period from 0 to 18 minutes and 54 to 74 minutes, respectively, the control unit applied stimulation to the vagus nerve. Heart rate variability was substantially reduced, while an average heart rate of 80 beats per minute was maintained. (Baseline heart rate, without stimulation, was approximately 95 beats per minute.) During a second period and a fourth period from 18 to 54 minutes and 74 to 90 minutes, respectively, stimulation was discontinued, and, as a result, heart rate variability increased substantially, returning to normal values. Average heart rate during these non-stimulation periods increased to approximately 95 beats per minute (approximately baseline value). Thus, these experimental results demonstrate that the application of

vagal stimulation using some of the techniques described herein results in a substantial reduction in heart rate variability (p. 108, line 26 - p. 109, line 13, emphasis added).

Claims 1 and 41 have additionally been amended to add an epicardial fat pad as an alternative stimulation site. This amendment finds support on p. 28, lines 27-31, and p. 81, lines 27-29. Conforming amendments have been made to dependent claims 31-33 and 71-73.

Claims 1-3, 5-8, 10-36, and 38-40 have been amended to replace the phrase "adapted to" with "configured to."

Claims 3 and 43 have been amended to conform with the amendments to claims 1 and 41.

Claims 3, 5-8, 10-12, 15, 17, 21, 32, 36, 38-39, 45-48, 50, 52, 55, 57, 61, 72-73, and 78-79 were originally presented as dependent claims. These claims were recast as independent claims after they were found to recite allowable subject matter in the previous office action dated July 6, 2006. In the present amendment, these claims have been restored to their original dependent form, as discussed above.

Claims 15-20, 43, 55-60, 66, 71, 75, and 78-80 have been amended to more positively recite the elements of these claims.

Claims 4 and 44 have been canceled because they are of similar scope to pending claims 34 and 74.

New claims 119 and 125 replace claims 9 and 49, which were canceled and the features of which were incorporated in claim 1 and 41, as described above.

New claims 120 and 127 are similar to claim 37 and 77 as originally filed.

New claims 121 and 126 are similar to claim 3 and 43, without the recitation of the time period. Claims 3 and 43 have correspondingly been amended to depend from claims 121 and 126, respectively.

New claims 122 and 128 find support in the specification as least as follows: "For other applications, control unit 20 is configured to apply generally continuous stimulation (e.g., in a manner that produces a prolonged reduced level of heart rate variability)" (p. 104, lines 4-7).

New claims 123 and 129 recite the integral feedback controller originally recited in claims 35 and 75. Claims 35 and 75 have accordingly been amended to remove this controller.

New claims 124 and 130 find support in the specification at least as follows: "For some applications, in order to additionally reduce the heart rate, stimulation is applied using a target heart rate lower than the normal average heart rate of the subject" (p. 105, lines 26-29).

New claim 131 recites the features of originally filed claim 76, which was previously canceled.

Tamir Ben-David, et al.  
Serial No.: 10/719,659  
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Page 33

The title has been amended to better reflect the subject matter of the pending claims.

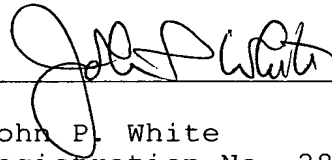
The Applicant believes the amendments and remarks presented hereinabove to be fully responsive to all of the grounds of rejection raised by the Examiner. In view of these amendments and remarks, the Applicant respectfully submits that all of the claims in the present application are now in order for allowance. Notice to this effect is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

Tamir Ben-David, et al.  
Serial No.: 10/719,659  
Filed: November 20, 2003  
Page 34

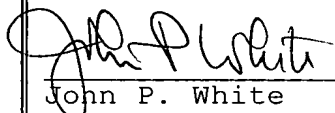
No fee, other than the total enclosed fee of \$120.00 for a one-month extension of time is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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